

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously presented) Method for the preparation of an antibody-tumor cell preparation for immunization of humans and animals against tumor cells comprising the steps of:

- a) isolating autologous tumor cells;
- b) treating the tumor cells to prevent the survival thereof following reinfusion;
- c) incubating the thus treated tumor cells with intact heterologous bispecific antibodies showing the following properties:
 - (i) binding to a T cell;
 - (ii) binding to at least one tumor-associated antigen on a tumor cell;
 - (iii) binding, by their Fc portion to Fc receptor-positive cells; and
 - (iv) capable of activating the Fc receptor-positive cell whereby the expression of cytokines, co-stimulatory antigens or both is induced or increased,

wherein the bispecific antibodies have isotype combinations selected from the group consisting of:

- rat-IgG2b/human-IgG1,
- rat-IgG2b/human-IgG2,
- rat-IgG2b/human-IgG3[oriental allotype G3m(st) = binding to protein A],
- rat-IgG2b/human-IgG4,
- rat-IgG2b/rat-IgG2c,

mouse-IgG2a/human-IgG3[caucasian allotypes G3m(b+g) = no binding to protein A, in the following indicated as *],

mouse-IgG2a/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2a/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2a/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2: > aa position 251]-human-IgG3*[CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge-CH2-CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG2-[hinge-CH2-CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG3-[hinge-CH2-CH3],
oriental allotype],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG4-[hinge-CH2-CH3],

human-IgG1/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG2/human-[VH-CH1,VL-CL]-human-IgG2-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

mouse-IgG2b/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

rat-IgG2b/mouse-IgG2a,

rat-IgG2b/mouse-IgG2b, and

rat-IgG2b/mouse-IgG3.

2. (Previously presented) Method according to claim 1, in which said antibodies are selected so that they are capable of binding Fc receptor-positive cells having a Fc γ receptor I, II, or III.

3. (Previously presented) Method according to claim 2, in which said Fc γ receptor I-positive cells are selected from the group consisting of monocytes, macrophages, dendritic cells, and activated neutrophils.

4. (Previously presented) Method according to claim 1, in which said antibodies are capable of inducing tumor-reactive complement-binding antibodies and thus inducing a humoral immune response.

5. (Previously presented) Method according to claim 1, in which said antibodies are selected to bind to the T cells via CD2, CD3, CD4, CD5, CD6, CD8, CD28 or CD44.

6. (Previously presented) Method according to claim 1, in which said antibodies are selected so that following their binding to the Fc receptor-positive cells the expression of CD40, CD80, CD86, ICAM-1 and/or LFA-3 as co-stimulatory antigens, and/or secretion of cytokines by the Fc receptor-positive cell is initiated or increased.

7. (Previously presented) Method according to claim 1, in which said antibodies are selected so that the secretion of IL-1, IL-2, IL-4, IL-6, IL-8, IL-12 being cytokines or of TNF- α or a combination thereof is increased.

8. (Previously presented) Method according to claim 1, in which said bispecific antibody is selected to be an anti-CD3 X anti-tumor-associated antigen antibody or anti-CD4 X anti-tumor-associated antigen antibody or anti-CD5 X anti-tumor-associated antigen antibody or anti-CD6 X anti-tumor-associated antigen antibody or anti-CD8 X anti-tumor-associated antigen antibody or anti-CD2 X anti-tumor-associated antigen antibody or anti-CD28 X anti-tumor-associated antigen antibody or anti-CD44 X anti-tumor-associated antigen antibody.

9-12. (Canceled)

13. (Previously presented) A method for preparing a vaccine comprising an antibody-tumor cell preparation, said method comprising preparing an antibody-tumor cell preparation by the method of claim 1, and preparing a vaccine from said antibody-tumor cell preparation.

14. (Currently amended) A method for preparing a vaccine comprising activated peripheral blood mononucleated cells, said method comprising preparing an antibody-tumor cell preparation by the method of claim 1 in which step (c) is replaced with step (d), which comprises incubating the thus-treated tumor cells with both ~~said~~ intact heterologous bispecific antibodies and peripheral blood mononucleated cells, thereby activating said peripheral blood mononucleated cells, and preparing a vaccine from the thus-activated peripheral blood mononucleated cells, wherein said intact heterologous bispecific antibodies have the following properties:

- (i) binding to a T cell;
- (ii) binding to at least one tumor-associated antigen on a tumor cell;
- (iii) binding, by their Fc portion to Fc receptor-positive cells; and

(iv) capable of activating the Fc receptor-positive cell whereby the expression of cytokines, co-stimulatory antigens or both is induced or increased,

and said bispecific antibodies have isotype combinations selected from the group consisting of:

rat-IgG2b/human-IgG1,

rat-IgG2b/human-IgG2,

rat-IgG2b/human-IgG3[oriental allotype G3m(st) = binding to protein A],

rat-IgG2b/human-IgG4,

rat-IgG2b/rat-IgG2c,

mouse-IgG2a/human-IgG3[caucasian allotypes G3m(b+g) = no binding to protein A, in the following indicated as *],

mouse-IgG2a/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2a/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2a/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2: > aa position 251]-human-IgG3*[CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge-CH2-CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG2-[hinge-CH2-CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG3-[hinge-CH2-CH3,
oriental allotype],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG4-[hinge-CH2-CH3],

human-IgG1/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-
IgG3*-[CH2-CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-
terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-
human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-
IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position
251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-
terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-
human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-
IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position
251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-
[CH2-CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-
IgG3*-[CH2-CH3],

human-IgG2/human-[VH-CH1,VL-CL]-human-IgG2-[hinge]-human-
IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-
IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

mouse-IgG2b/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

rat-IgG2b/mouse-IgG2a,

rat-IgG2b/mouse-IgG2b, and

rat-IgG2b/mouse-IgG3.

15. (Previously presented) Method according to claim 1, in which said tumor cells are incubated with the antibodies for a period of 10 minutes to 5 hours.

16. (Previously presented) Method according to claim 1, in which said tumor cells are incubated with the antibodies for a period of 15 minutes to 120 minutes.

17. (Previously presented) Method according to claim 14 in which said incubation of step (d) is performed for a period of 1 to 14 days.

18. (Previously presented) Method according to claim 14 in which said incubation of step (d) is performed with about 10^8 to 10^{10} mononucleated peripheral cells.

19. (Previously presented) Method according to claim 1, in which said tumor cells are present in the amount of about 10^7 to 10^9 cells.

20. (Previously presented) Method according to claim 1, in which said bispecific antibodies are added in an amount of 2 to 100 μg .

21. (Previously presented) Method according to claim 1, in which said treating of the tumor cells in step b is performed by irradiation.

22. (Canceled)

23. (Currently amended) Method for preventing the reoccurrence of a tumor, said method comprising administering an antibody-tumor cell preparation prepared according to the method of claim 1 to an individual in whom ~~such~~ tumor cells have ~~appeared~~ reappeared ~~an antibody-tumor cell preparation prepared according to the method of claim 1~~.

24-25. (Canceled)

26. (Previously presented) A pharmaceutical composition comprising an antibody-tumor cell preparation obtained by the method of claim 1.

27-31. (Canceled)

32. (Currently amended) A method for preventing the recurrence of a tumor, said method comprising: preparing an antibody-tumor cell preparation by the method of claim 1 in which step (c) is replaced with step (d), which comprises incubating the thus-treated tumor cells with both ~~said~~ intact heterologous bispecific antibodies and peripheral blood mononucleated cells, thereby activating said peripheral blood

mononucleated cells; and administering to an individual in whom ~~such~~ tumor cells have ~~appeared~~ reappeared the activated peripheral blood mononucleated cells, wherein said intact heterologous bispecific antibodies have the following properties:

- (i) binding to a T cell;
- (ii) binding to at least one tumor-associated antigen on a tumor cell;
- (iii) binding, by their Fc portion to Fc receptor-positive cells; and
- (iv) capable of activating the Fc receptor-positive cell whereby the expression of cytokines, co-stimulatory antigens or both is induced or increased,

and said bispecific antibodies have isotype combinations selected from the group consisting of:

rat-IgG2b/human-IgG1,
rat-IgG2b/human-IgG2,
rat-IgG2b/human-IgG3[oriental allotype G3m(st) = binding to protein A],
rat-IgG2b/human-IgG4,
rat-IgG2b/rat-IgG2c,
mouse-IgG2a/human-IgG3[caucasian allotypes G3m(b+g) = no binding to protein A, in the following indicated as *],
mouse-IgG2a/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],
mouse-IgG2a/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],
mouse-IgG2a/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],
mouse-[VH-CH1,VL-CL]-human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2: > aa position 251]-human-IgG3*[CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge-CH2-CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG2-[hinge-CH2-CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG3-[hinge-CH2-CH3, oriental allotype],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG4-[hinge-CH2-CH3],

human-IgG1/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG2/human-[VH-CH1,VL-CL]-human-IgG2-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

mouse-IgG2b/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

rat-IgG2b/mouse-IgG2a,

rat-IgG2b/mouse-IgG2b, and

rat-IgG2b/mouse-IgG3.

33. (Previously presented) The method of claim 32, wherein the peripheral blood mononucleated cells are added following a preincubation of the thus-treated tumor cells with said intact heterologous bispecific antibodies.

34. (Previously presented) The method of claim 14, wherein the peripheral blood mononucleated cells are added following a preincubation of the thus-treated tumor cells with said intact heterologous bispecific antibodies.

35. (Canceled)